REMARKS

Claims 6-9, 12, 14, 17, and 22 are cancelled, claims 6-9, 12, 14, and 17 being drawn to non-elected inventions. Claim 1 is amended. This amendment is supported throughout the application as filed, e.g., at page 1, lines 20-24. No new matter is added. Claims 1-3, 5, 10, 11, 13, 20, 21, 23, and 24 are pending and under examination.

A Declaration of Dr. Katia Georgopoulos (unsigned) was filed along with an amendment and response on March 29, 2002. The executed declaration, which is identical to the previously submitted unsigned version, is submitted herein. Applicants apologize for the inconvenience.

Rejection Under U.S.C. 112, First Paragraph

Written Description

Claims 1, 3, 5, 10, 11, 13, and 20-24 are rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner contends that nucleic acid sequences encoding a Helios protein other than that set forth in SEQ ID NO:6 fails to meet the written description requirements. In support of this contention, the Examiner asserts the following:

> In the instant case, there is adequate written description for any inherent property of the protein for SEQ ID NO:6, however the specification does not teach how to maintain the inherent properties with any modification to the Helios protein. It is noted that the specification sets forth the particular embodiments recited in the claims, however the specification fails to provide any clear guidance on the specific changes one can make and maintain the recited biological activities.

The rejection has been met, in part, by amending claim 1 to increase the required percent identity to 90%. The rejection is respectfully traversed with regard to the pending claims as they fully satisfy the written description requirement under Federal Circuit law as well as the Patent Office's own Written Description Guidelines (the Guidelines) cited by the Examiner. Written description can be satisfied as follows:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (Federal Register, Vol. 66, No. 4, at page 1106.)

The present claims clearly meet this standard. The claimed nucleic acids are limited structurally in that they have a very high degree of identity with SED ID NO:6 (e.g., 90% or differing by 1 or more residues, but less than 15 residues) or hybridize under high stringency conditions to a recited reference sequence. They are also limited functionally in that they must encode an amino acid sequence having one or more of the following transcription factor functions: (a) the ability to form a dimer with a Helios, Aiolos or Ikaros polypeptide, (b) the ability to bind DNA, and (c) the ability to stimulate transcription from an Ikaros binding site.

With regard to claims 3 and 5 in particular, the Examiner is directed to Example 9 of the Synopsis of Application of Written Description Guidelines (the Synopsis of Application), indicating that claims very similar to claims 3 and 5 are adequately described. Furthermore, the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe Inc.* (296 F.3d 1316, Fed. Cir. 2002), has taken judicial notice of the Guidelines and the Synopsis. Specifically, the Court refers to Example 9, stating that genus claims to nucleic acids based on their hybridization properties may be adequately described if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar. (*Enzo*, 296 F.3d 1316 at 1327.) Similarly, with respect to claims 1 and 20, proteins having at least 90% sequence identity to (or differing at fewer than 15 residues from) SEQ ID NO:6 will be structurally very similar.

While Applicants believe the above arguments are sufficient to overcome the written description rejection, the Examiner's specific concerns will be addressed in turn. For example, the Examiner asserts the following:

> Besides a general comparison, the specification fails to clearly indicate which amino acids are necessary for any given activity or which ones can be changed without consequence to the activity.

Applicants disagree. As Dr. Georgopoulos, one of the co-inventors, clearly states in her declaration of April 10, 2002 ("Declaration"), Figure 1 of the specification, together with the accompanying legend (page 35, lines 19-24) shows the structure and placement of the various domains and zinc finger motifs of the Helios protein. Additionally, page 62, lines 17-19 of the specification provide that "strong conservation of the N-terminal zinc finger motifs of Hel-1 and Hel-2 with Ikaros isoforms Ik-1 and Ik-2 predicts that they will display similar affinities and DNA binding specificities." This prediction was confirmed on page 72, lines 5-19 of the specification wherein Helios was tested for its ability to activate transcription from the Ikaros binding sites. These results confirmed the functional conservation of both the DNA binding and transcriptional activation domains. One of skill in the art, upon identification of functional domains of a protein, as provided in the specification, would be able to predict which amino acid changes would be necessary for any given activity.

Applicants also disagree with the Examiner's assertion that without the detailed experiments performed like those of other Ikaros family members, one cannot predict the role or function of Helios. The specification provides clear and adequate support for Helios' role as a transcription factor (See e.g., page 72, lines 5-19.). Furthermore, the Examiner overestimates the difficulty in predicting the related functions of the Helios polypeptide. As the inventor clearly indicates in her Declaration:

> Accordingly, one of ordinary skill in the art could easily predict that deleting or mutation the 4 N-terminal zinc finger region in Helios would abolish its DNA binding activity and would not affect dimerization activity. One could also predict that mutating or deleting only some of the Zinc fingers in Helios would affect sequence specificities and affinities for DNA (as in Ikaros) while not completely abolishing DNA binding (page 5, paragraph 11).

The Examiner asserts that Dr. Georgopoulos' declaration is unpersuasive because

> the written description requires more than a mere indication of potential limitations. A comparison of family members may provide the basis for determining conserved sequences, however,

> this does not provide any evidence that they are responsible for any particular biological activity.

Again, Applicants disagree. The Declaration together with the specification provide for much more than a mere indication of potential limitations. Specifically, page 3, paragraph 7 of the Declaration (see also, page 72, lines 5-19 of the specification) confirms Helios function as a transcription factor, using a reporter gene to test its function. Page 3, paragraph 9 of the Declaration (see also the paragraph bridging pages 69-70 of the specification) discusses the structural features of Helios that are responsible for the formation of homo and heterodimers. And, page 5, paragraph 11 of the Declaration describes the role of the 4- N-terminal zinc finger region with respect to DNA binding.

Furthermore, while the structure and function of Helios is compared to family members, this sort of comparison is the type done regularly by one of skill in the art, as declared below:

> Given the degree of structural similary between Ikaros and Helios, the domains of the Helios protein can be predicted to function in a manner similar or analogous to the domains of Ikaros. In fact, I have not performed analogous experiments with Helios precisely because I believe that the results of the Ikaros experiments with regard to basic structure and function extend to Helios as well. (Page 4, paragraph 10 of the Declaration)

Thus, it appears that the Examiner has not fully considered the evidence presented by Dr. Georgopoulos' declaration, that the similarity between Ikaros and Helios, coupled with the functional data on Helios presented in the specification, provides sufficient evidence that Applicant's were in possession of the full scope of the claims.

Finally, the Examiner cites *The Regents of the University of California v. Eli Lilly and Company* (119 F3d 1559, Fed. Cir. 1997) to support the assertion that the present claims do not meet the requirements for written description. However, the claims in *Eli Lily* are sufficiently distinct from the claims of the present invention. In *Eli Lily*, it was attempted to claim human insulin-encoding DNA based solely on a functional limitation. More specifically, the claims in *Eli Lily* are similar to Example 17 in the Synopsis, wherein the PTO suggests the claims are not adequately described. In contrast, in the present case, the claims recite structural and functional limitations. As noted above, the claims of the present invention are very similar to Example 9,

wherein the PTO suggests the claims are adequately described. As dicussed above, the Court in *Enzo* took judicial notice of the Examples provided in the Synopsis of Application.

In view of the foregoing, the specification provides ample disclosure of specific, common structural features as well as functional features that serve to distinguish the claimed nucleic acids from those nucleic acids falling outside of the claims. Accordingly, the requirements of 35 U.S.C. §112, paragraph 1, are satisfied.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants ask that all claims be allowed. Enclosed is a Petition for Extension of Time along with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 10287-043001.

Respectfully submitted,

Date: 22 November 2002

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Version with markings to show changes made

In the claims:

Claims 6-9, 12, 14, 17, and 22 have been cancelled.

Claim 1 has been amended as follows:

1. (Thrice Amended) A substantially pure nucleic acid comprising a nucleotide sequence which encodes an amino acid sequence that is at least [80%]90% identical to the amino acid sequence of SEQ ID NO:6, and which encodes a polypeptide having one or more Helios biological activity selected from the group consisting of:

(d) the ability to form a dimer with a Helios, Aiolos or Ikaros polypeptide;

(e) the ability to bind DNA; and

(f) the ability to stimulate transcription from an Ikaros binding site.